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Toxicology in Tables

4td Year

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General toxicology

**** Factors affecting toxicity of drug**

A) Drug : state (conc-form-solubility-PH) – Dose – Route – cummulation –interaction – metabolism

B) Patient : stomach (PH-amount of food – type)- age – health /// allergy-idiosyncry-tolerance

**** Investigations :**

1- Samples : blood –urine-stool-vomitu-hair-nail //// stomach – liver-kidney

2- Routine : CBC – electrolytes-PH- ABG +_ liver function & kidney function & ECG

3- Search for poion or its metabolites

**** PMP :**

1- *stomach* (SUS) smell : phenol – opium-cyanide /// ulcer : corrosives // seeds

2- *skin* : SES smell // eshers black in sulphric & yellow in nitric & brown in phenol // site of injection

3- *brain* : edema & congestion

4- *passages* : asphyxia (barbiturates – opium-CO-HCN)

5- *PMP* : hypostasis : deep blue in asphyxia & brown in nitrates & red in CO & CN

RM : early in convulsions (strychinine)

Putrefaction : late in dehydration (arsenic)

**** Treatment** :

A) supportive :

1- airway : head & tongue & FB & tubes **2- Breathing** : face mask & nasal canula & mechanical respiration

3- circulation : IV fluids & vasopressors – inotropics & Antiarrhysmic drugs

4- CNS: coma cocktail : dextrose 50 ml 50 % solution & thiamine 100mg IV & naloxone 2mg IV

B) GIT decontamination :

1- Emesis : done in all within 3 hours except :

CNS proplems (coma & convulsions) --- CVS PROPLEMS electrolytes imbalance --- GIT proplems (varice s-recent operation) ---- infant below 6 months and neurologically impaired /// chronic poisoning – corrosives – volatile hydrocarbons – rapid onset of CNS depression

2- Gastric lavage : same contra of emesis but it can be done in coma & volatile hydrocarbons (cuffed tube) – convulsions (general anaesthesia)

Done within 3 hours but can be done up to 12 hours in 1- sticky poisons (salicylates) 2- slow gastric motility (barbiturates) 3- secreted in stomach (morphine)

3- Cathertics : not used in 1- corrosives 2- osmotic in RF 3- oil in fat soluble poisons as pesticides

4- Whole bowel irrigation : done in 1- poorly absorbed poisons 2- preparations slow release 3- packets of illicit drugs (cocaine & heroin)

C) Local antidote :

1- Activated charcoal : work for all except

1- ineffective with

C→ cyanide & corrosives

H→ heavy metals

A→ Alcohol

R → Rapid absorption & onset

C→ Chlorine & Iodine

O→ others insoluble in water

A→Aliphatic & Hydrocarbons

L→ Laxatives (Na-Mg-K)

2- obstruction 3- adynamic ileus 4- lack of airway protection (coma 5- with oral antidotes (NAC – DMSA – penicilamine)

Dose : 50-100 gm orally with H_2O

2- MDAC : done in :

1-enterohepatic circulation (TCA – digitalis – barbiturates)

2- sticky : salicylates 3- slow gut motility (Barbiturates- morphine –anticholinergic)

Dose : 0.5-1 gm/kg /4hrs

3- Demulcent : milk & egg white coating the mucosa

4- Entanglers : cotton for solid object

5- Dissolvant : Ethanol 10 % for phenol then rapid irrigation

6- Precipitation :

Ca for oxalic acid -

$MgSO_4$ → lead

Skimmed milk →mercury

Tannic acid for plants

7- Reduction :

Mercuric by Na formaldehyde sulfoxalate → Mercurous non toxi

8- Oxidation :

H_2O_2 & $KMnO_4$ for plants & cyanide

D-elimination of Poison from blood

1- Forced dieresis &ion trapping :

a)Osmotic b ymannitol 20 % & fluid by glucose + saline

B) Ion trapping :

1-alkaline dieresis : for acidic drugs as salicylate by \NaHCO3 1-2 mg/kg in 5 % dextrose

2- Acidic dieresis : for alkaline drugs as amphetamine by NH_4Cl 75 mg/kg in 5% dextrose

2- Dialysis (hemo & peritoneal)

3- Hemoperfusion : not if toxin not adsobable to charcoal

4- plamapheresis

E- Physiological antidote

Chelators for metals

1- BAL (2.5 62 121)

2.5 mg/kg/6hr for 2 days

Then 2.5mg/kg/12hr for 1 week

2- DMSA (10 85 122)

10mg/kg/8hr for 5 days then

10mg/kg/12hr for 2 weeks

3- EDTA (125)

1 gm twice daily for 5 days iv infusion

4- penicillamine : 250 mg / 6 hr for 20 days

5- Desferal : for iron 0.5 gm/4hr for 2 days

F- Symptomatic

1- cerebral edema :

Mannitol + cortisol

2- Pulmonaary edema :

Mannitol + cortisol + suction + O_2 under pressure

3- convulsions

Diazepam + sedatives / succinylcholine 10 mg Iv – $MgSO_4$ Im

4- Liver failure :

↓ Ptn & ↑ glucose & vit K & electrolytes Ca gluconate + glutathione

**** Clinical picture**

1- GIT : N& V&C&D

2- Heart : ↓pulse &↓ Bp then arrest ***3- Motor*** : ↑→↓ : twitches & tremors & convulsions → paralysis

4- CNS ↑ : CHAIR (convulsions – HTN & anxiety & irritability & restlessnss)

5- CNS ↓ : cyanosis & coma & central asphyxia

6- Renal failure : oliguria + ABC + Anuria

7- liver failure : pain & tenderness in right hypochondrium & jaundice e+ bleeding & ↑ billirubin & SGOT & SGPT __ ↓ Albumin & prothrombin

	Atropine	Morphine	Digitalis	Cannabis	Cocaine	Strychinine
sources	Datura fastiosa & stramonium – atropa belladona	papaversomniferum → opium	digitalis purpura – lanata – sea squill –oleander	cannabis sativa & cannabis indica in flower tips or dried leaves or mixed	leaves of Eyrthroxylon coca plant	strychnos nux vomica
uses	Mydriatic- BD- antagonist for (morphine-digitalis- organophosphorus)	pain killer – ttt of drug addict	congestive HF – Atrial arryhthmia	smoked – ingested- inhaled – tablets in drug abuse	local ana – antiarrhythmic – sports doping – drug abuse (sniffing – smoking – injected)	Rodenticide
Active principles	Atropine-hyocyamine- hyoscine	opium – morphine – codaeine	Digoxin – digitoxin-digitalin	delta-9-tetra hydro cannabinol	Cocaine	Strychinine & Brucine
condition	Accidental (children- addict or eating manzool)- homicidal (road poison)	Accidental in addicts	Acute – chronic therapeutic accidental	accidental by addicts	Accidental overdose in addicts or anaesthesia	Very rare in suicidal and homicidal Quick-very painful- very bitter
Mechanism	1-atropine : -central : CNS ++ then -- & peripheral anti muscurinic 2- hyoscine : CNS depression from start & no peripheral aaction	act on opiod receptors mu- delta-kappa not sigma → euphoria + analgesia	1-elongate diastolic period 2-enforce systolic pwer 3-↑ renal blood flow by ↓Na K Atpase →↑Na&Ca intracellular & ↓K extra	THC stimulates sympathetic and ↓parasympathetisc & CNS stimulation or depression according to mood – concentration- route	1-sympathomimetic & strong CNS stimulant 2- Local anaesthetic	block glycine receptors in ventral horn cells lead to simultaneous contractions of allmuscles of the body
C/P	1-Dry as abone : -- saliva – lacrimations - sweat & bronchial secretions 2- blind : dilated fixed pupil 3- red : flushed skin 4- hot : atroppine fever 5- bladder : -- motility 6 –heart : tachycardia 7- mad : occupitional delerium & drunken gait	1- CNS : euphoria –stupor → coma & death 2-CVS : ↓ collapse 3-Resp : ↓ RC 4- cough ↓ non cardiogenic pulonary edema 5- HRC ↓ hypothermia 6- Miosis & constipation 7- withdrawal sypmtoms after 6-12 hs of stop	1-Dysarrhythmai: brady- tachy 2-Diarrhea & N-V-C 3-Dyevision : yellow – green 4- Delirim- Disorientation	A)MENTAL : 1- Euphoria then Dysphoria 2-sexual or erotic dreams 3-↑ special senses as touch 4- Disorientation of time 5- Disorientation of space B)PHYSICAL : as atropine (Blind – heart- dry – bladder + conj congestion – ortho hypotension -↑appatite & urine	A)CNS : ↑→↓ 1-↑ (EUphoria &↑ motor →exagoratted reflexes & ↑HRC →hyperthermia &↑ RC → ↑ resp depth) 2- ↓ loss of reflexes & ↓ resp & coma & cyanosis & death B) CVS : ↑ BP – Arrhythmia – coronary artery spasm – collapse C) renal failure – coke burn – perforation of nasal septum in chronic	*A-muscular stiffness & cramps :* 1-risus sardonicus 2-opisthotones position 3- cyanosis & conscious *B- Postictal depression* &sleep and any stimuls lead to new attack c- Lactic acidosis & HTN & fever & N – V – D
Cause of death	respiratory depression 1st 24 hs	central asphyxia – pulmonary edema – arrhythmia – irreversible brain damage	Arrhythmia – cardiac arrest	Central asphyxia & car accidents	HYPERTHERMIA – central asphyxia – circulatory collapse	Asphyxia - in attacks (spasm of respiratory muscles) – in between (Exhaustion resp muscles or RC)
investigation	chemical analysis (tropin + tropic acid)	1-morphine + meconic acid 2-chest Xray for edema	1-electrolyte level K- Ca – Mg 2-Digoxin level ≥ 2 ng	detect THC in blood & urine samples upto 45 day	1- detection of benzoylecgonine in urine by HPLC OR GC up to 2-3 days 2- serum enzymes CPK-AST- ALT)	1- strychinine level in urine & gastric by HPLC & GC 2- CPK↑
D/D	from alcohol (smell – vomiting- moist skin – Mcwen sign – decrease temp)	(coma – cyanosis – constriction) carbolic acid – organo phosphorus – pontine hge				1- Tetanus (history- bacteria – Lock jaw –hypertonia in between) 2-Epilepsy (history- loss of consicious)
TREATMENT	1-No suction in ABC 2- lavage up to 12 hours 3- physiological : pilocarpine 10 mg IV & physostigmine 1- 4mg IV 4- catheter & Enema for constipation & cold foment for fever & convulsive ttt in stimulation & Caffeine in depression	1-cuffed endotracheal tube even if alert 2-lavage even if injected 3-Anti : Atropine 1 mg iv & Naloxone 0.4 -2 mg – 1 hr & nalmefene 1-2 mg – 8 hr & Naltrexone 0.1 -0.4 mg – 72 h	1-prevent further exposure 2-treat arrhythmia by electrolytes (insulin in glucose in ↑K in acute & KCL in chronic) and Antiarrhythmic (Atropine 1 mg IV & lidocaine 1mg /kg) 3- Digibind (specific antidote) if serum level > 10 ng /ml or ingestion > 10 mg – or heart block → it reverse tissue binding	1-No specific antidote 2- mild sedation 3- Psychatric follow up 4- Reassurance	1- stimulation (chlorepromazine – lithim – diazepam- cool quite environment) 2- HTN : alpha blocker 3- hyperthermia : chlorepromazine + salicylate 4- forced acidic diuresis is now contra	1-quite environment dark 2-anticonvulsant : Diazepam 0.1 mg/kg IV & Pancuronium 0.1 mg/kg IV 3- Emissi is contra & Lavage is done under general anaesthesia 4- IV $NaHCO_3$ for lactic acidosis

	Inorganic acids	Inorganic alkalis	Carbolic acid (phenol	Oxalic acid	Acute Lead	Chronic lead
sources	Automobile battery-metal cleanear – toilet boil cleaner	House hold bleaches – detergent - cement	Coal car derivative	Metal polish	1- oral : children pica – water-ceramic food containers 2-inhalation : Pb fumes – TEL 3- Dermal : cosmetics – petroleum additives $ -IV : metamphetamine users	***Kinetics :*** - Absorption : children absorb more – skin – Ca-Zn-Fe ↓its absorption & Vit D ↑ deposition & Parathyroid ↑release/// - Distr: in bone – teeth-hair& Bone 90% total lead /// Exe : renal 75% - Bile-sweat –exofoliated epithelium &1/2 life 30year in bone – 7 years in kidney
Active principles	H_2SO_4- HCL – HNO_3	NaOH-KOH-K_2CO_3	Carbolic			
uses	H_2SO_4→ battery HCL→dye manufacturing & HNO_3 → fertilizer manufacturing		Disinfectant in Dettol – Lysol – phenol	Remove ink stain		
condition	Mainly accidental – in homicidal for disfigurement	Accidental as potash k_2co_3 simulate milk in color	Suicidal (easy obtained – cheap-painless) - never in homicidal for character smell	Accidental as it is mistaken for sugar or salt – occupational	Mainly accidental (lead oleate in criminal abortion – Tel- suicidal by insecticide	
Mechanism	Coagulative necrosis causes sever ulcers → perforation stomach- skin eschars- edema of respiratory passages	Liquefactive necrosis causes sever ulcers →stricture of esophagus – skin eschars-asphyxia	**1) Local :** (stomach) mid corrosive sup ulcers – coagulative necrosis theckining of mucosa – local anaesthesia (skin) eschers – local anaesthetic **2) Remote** : CNS ↑→↓ & CVS ↓ & RES : Resp alkalosis then metabolic acidosis & Methemoglobinemia & acute glomerulonephritis	***1) local*** : superficial ulcers & eschers ***2) remote*** : Ca oxalate crystals → 1- renal failure 2- hypocalcemia : → 1- cardiac arrest 2- tetany (peripheral) 3- convulsions central	-Combine with SH group on ptn in brain –blood-PNS – kidney - combine with SH group of enzymes of : ↓ of enzymes of heme synthesis → anemia & ↓↓ pyridine -5- nucleotidase → clumping of ribosomal RNA (basophilic stippling)	***1-Buccal*** :blue line at gingival margin ($H_2S+Pb=PbS$ blue) ***2- Bowel*** : Colic relived by pressure - constipation ***3- Blood*** : Microcytiic hypochromic anemia – circum oral pallor- punctuate basophillia- Reticulocytosis ***4- Brain*** : Lead palsy on extensor side–Encephalopathy ***5- Bone*** : Arthartic pian – lead lines 6- Productive : abortion –sterility-impotance ***7-Renal :*** Fanconi like syndro
C/P	1-**<u>ingestion</u>** sever pain from mouth to stomach →dysarthria – dysphagia & Black vomiting contain acidic hematin → constipation + dehydration which lead to shock and oliguria 2- **Inhalation :** edema glottis → asphyxia 3- **Skin** : Eschars black (H_2SO_4) – RED (HCL) – YELLOW (HNO_3)	Same as acids but 1-in ingestion : Vomiting → soapy white As contain alkaline hematin Diarrhea soapy white 2- inhalation : severer asphyxia NH_3 3- skin : white eschars	**<u>1) Local</u>** : (stomach) pain +vomiting withsmell temporary du to anaesthesia (skin) brown eschers **<u>2) Remote :</u>** - CNS : ↑→↓ + constricted pupil - CVS : collapse - Kidney : acute glomerulonephritis & urine turn green on exposure to air	***1) Local*** : pain + vomiting of white crystals & white eschars ***2) REMOTE :*** 1- renal failure & Ca oxalate crystals in urine 2- hypocalcemia → 1- contraction of face and extremities)carpopedal spam 2- contraction of resp muscles Resp failure 3- cardiac asystole 4- convulsions	***1-GIT*** :N-V-C metallic taste – constipation with black offensive stools PbS ***2- Renal*** : Fanconi like syndrome (aminoaciduria-phosphaturia – glucosuria – ABC in urine) ***3- Nervous*** : Encephalopathy –parathesia –coma – convulsions – mental changes	
Cause of death	S→neurogenic shock immediate A→Asphyxia in few hours D→ dehydration & shock in 12hours P→ perforation of stomach in days(more in acids) C→ cachexiadue to etricture in weeks (more in alkalis)		4RF → (resp failure in 4 hrs) (Renal failure in 4 days)	1- peripheral asphyxia in 15 min 2- obstructive renal failure in few hours 3- cardiac arrest in diastole	Renal failure – central asphyxia	1- blood leadleval : > 55μg/dl indicate toxicity 2- blood picture : anemia – reticulocytosis- stippling 3- X-ray bone : lead lines increase on plonged exposure 4- Urine analysis :↑ ALA due to ↓ALA dehydra
investigation	1-Abdominal X-ray → perforation 2- fibroptic endoscopy →grades from 0 to III (no lesion-erythema& edema -ulceration-transmural involvement)		1- urine analysis (green & hemoglobinuria) 2- methemoglobin level	1- Ca oxalate crystals in urine 2- Ca level in blood	Pb leval in blood	
D/D				Arsenic differentiated by Reinsch test +ve in arsenic		
TREATMENT	1) **Inhalation :** care of respiration **2) skin** : wash with water & antibiotic oint +- skingraft **3) ingestion :** ***1- supportive :*** ABC + pain killer for neurogenic shock & surgical as gastrectomy in perforation & in cachexia → colon by pass or bougienage ***2- GIT decontamination*** : No emisis – no lavage for fear of perforation & No neutralization for fear of perforation and stomach rupture due to exothermic heat reaction and CO_2 production ***3- Local antidote : 2 glasses of milk*** or egg white as demulcent & No charcoal – Give H2 blocker to ↓ HCL production ***4- symptomatic*** : steroids to prevent fibrosis		1)***Decontamination:*** No emesis (rapid coma – corrosive effect) = Lavage is essential (vomit is temporary – thickeneing of mucosa so no perforation – it has remote action) 2) ***Local :*** milk & egg white (it coagulate their ptns) – ethanol 10 % (dissolvent) 3)***Symptomatic :*** vit C or methylene blue for methem-oglobinemia more than 30%	***<u>Ca is life saving</u>*** ***1- local antidote*** : milk & $Ca(OH)_2$ →precipitate oxalic ***2- physiologic*** : Ca gluconate 10% slowly IV or orally ***3- Symptomatic*** : Diazepam for convulsion & IV fluids to prevent Ca oxalate crystals prcipitatin in kidney	***1- supportive*** : Ca gluconate for Pb colic – Mannitol for ↑ICT ***2- Local*** : $MgSO_4$ & no charcoal ***3- Physiological*** : all chelators ex desferal (Ca-Na_2 EDTA – BAL – DMSA-DMPS-penicillamine)	1- Prophylactic : periodic examination – protective clothing – masks-gloves – proper ventilation – proper amounts of Ca-Zn-Fe 2- Remove from further exp 3- Chelating agents as acute 4- Symptomatic : $MgSO_4$ for constipation – Fe for anemia – Diazepam for convulsions – splint & massage for wrist drop

	Acute mercury	Chronic mercury	Acute arsenic	Chronic arsenic	Cadmium	Iron Acute
sources	1- metallic mercury: medical instrument – inhalation only 2- inorganic : mercurous Cl cause acrodynia & Mercuric Cl disinfectant & Mercurial fulminate percussion cap & mercurial cyanide insecticide 3- organic ; aquatic food		Organic & Inorganic(pentavalent & trivalent) higher valency – less toxic & arsine gas is product of ore smelting		Zn & lead smelting – cigratte smoking- coal- electroplating	Synthesis of hemoglobin – myoglobin - cytochromes
uses			Pesticide –wood persative –manufacturing of glass – arsine gas used in semiconductor industry & contaminate well water		Photography – fireworks – plastics as polyvinyl chloride	Widely in ttt of anemia – common daily vitamin supply
condition	Accidental : by mercuric chloride – rare in others		1- homicidal : common due to no smwllor taste & different color – early syptomts are gastroenteritis after 1-4 hrs but detected after putrefaction 2- accidental : cooking utensils by copper ore & workers in paints – wallpaper by arsenie gas - rare suicidal (very painful l)		Accidental or occupational exposure	Mainly accidental - iron preparation s come in attractive forms similar to candies – availablein home
Mechanism	React with SH group →↓ cellular enzymatic mechanism – metallic & organic are toxic to CNS but inorganic are nephrotoxic		General protoplasmic poison combine with SH containing enzymes of oxidation – reduction →uncoupling →energy block	Execretion : in urine ½ h afterabsorption – in descending colon – in sweat & milk	1-Combine with SH containing enzymes especially α1 antitrypsin→ emphysema 2- compete with cellular uptake of Cu-Zn	**Local** : corrosive effect **Remote** : Liver Pperiportal necrosis /// CVS : shock – hypotensin /// metabolism : metabolic acidosis
C/P	1- GIT : burning sensation from mouthto stomach & blood tinged vomiting – Mercurial dysentery 2- renal : acute toxic glomerulonephritis 3- corrosive bronchitis & pulmonary edema 4- Nervous : tremors & ↑ excitability	1- Eye : Mercurialentis 2- skin : oozing dermatitis 3- Renal : renal failure 4- Intestinal : Mercurial dysentery 5- oral : salivation –grey line –gingivitis –cancrum oris 6- Nervous : Kinetic tremors 7- psychic : Hg erethism)shyness- vague fear – depression)	1-GIT : rice-water stool - N-V-C-D & dehydration – collapse – garlic odour of breathand sweat 2- Remote action : damage of organs →hepatic –cardiac – renal failure 3- arsine ga s: hemolytic anemia – hemoglobinuria – renal failure	1- A : aplastic anemia : with basophilic stippling 2- S : Skin : Melanosis – hyperkeratosis –alopecia – warts . 3- N ; peripheral neuritis : mixed but more sensory 4- C : Coryzaal ike : cough-lancation-hoarsness of voice – perforation of nasal septum 5- parynchematous degeration fatty liver –renal failure - HF	More toxic if inhaled than swallowed ACUTE : ingestion : P-N-V-C-D Selflimmited /// inhalation : pulmonary edema – respiratory failure – bilateral cortical kidney necrosis CHRONIC: kidney : Fanconi syndrome // lung : COPD – cancer /// bone : osteomamacia /// yellow coloration of teeth & testicular damage	***Stage 1*** : 1 hr : corrosive effect on GIT →hematemsis-melena ***Stage 2 :*** 1 day : apparent recovery ; due to redistribution of free iron ***Stage 3*** : 2 days ; ALL : corrosive effect- collapse – hepatic necrosis –metabolic acidosis- coma ***Stage 4*** : 2 weeks : gastrointestinal scarring and obstruction
Cause of death	Dehydration 1 day & renal failure 1 week				Respiratory failure	1- hepatic necrosis – renal failure
investigation			1- Reinch test in GIT –viscera – nails 2- atomic absorption spectrometry	Reinch or atomic absorption spectrometry in bone –teeth-nail-hair	Cd stored in liver & kidney due to high level of metallothionein (metal binding protein)	**1- abdominal X-ray** : see iron tab --- 2- Deferoxamine challenge test
D/D			From cholera in which : fever-vomiting after diarrhea – no colic or tensmus – analysis reveals V.cholera and the revese of this is in arsenic			
TREATMENT	1- no further exposure 2- Lavage gu one of the local antidotes : egg white & skimmed milk →precipitatin / Na foemaldehyde sulphoxalate →reduction 3- chelating agents (no EDTA & desgeral) 4- renal care – IV fluids for dehydration	1- prophylactic 2- prevent further exposure 3- Chelating agents : BAL- DMSA- DMPS – Penicillamine 4- symptomatic : Mouth hygiene – tranquilizers – atropine for salivation – Na hydrosulphide or BAL oint for dermatitis	1- Lavage : using ferric hydroxide for precipitation as ferric arsenate & then leave olive oil or milk as demulcent 2- Chelating agents : all except EDTA 3- Syptomatic : IV fluids for dehydration Morphine for colicy pain Glucose & vitamins for liver *****PMP :*** gastic mucosa : large superficial ulcers with normal mucosa in between & degeneration of live r-heart-kidney & delayed putrefaction	1- prophylactic-prevention 2- Chelating agents 3- Sypmtomatic : Liver support : dextrose – vit Artificial kidney	Mainly preventive 1- protective & prevention 2- high Zn containing diet 3- chelation : effective oly in acute exposure – EDTA is chelator of choice – BAL should not be used as it make nephrotoxic complex	**1-** whole bowel irrigation 2- local anti : NaHCO3 convert free ferrous to ferrous carbonate 3- physiologic : Deferoxamine 4- NaHCO3 IV for acidosis *Mahmoud Behairy*

	Alcohol	Methanol	Hydrocarbons :	Carbon monoxide	Cyanide	Organophosphorous
sources	Fermentation of sugar	Distillation of wood	Petroleum distillates (gasoline-kerosine)- coal tar benzene) – pine wood turpentine	Incomplete combustion of carbon compounds as in cars exhaust – cigar- fires –coal mines-charcoal burning	1- industry in photography – plastic –fumigation 2- plant : amygladin in unripe fruit 3- med : nitroprusside-laetrile 4- house : acetonitraate in nail glue remover –cigratte smoking	In insecticides –herbicides-rodenticide
uses	Beverage-solvent- OTC as mouthwash preparations – cold&cough	Adulterated in alcohol – solvent-paint remover – cleaner	Lubricants- solvents – furnitures –fuels –paint remover	No uses also produced in our bodies in catabolism of hemoglobin		
condition	Accidental- homicidal to facilitate rape-roberry	Accidental	Accidental –inhalation abusers	Accidental in fires-coalmine workers- suicidal in automobile exhaust in closed	Accidental – suicidal in spies – homicidal excetion in gas chamber	Accidental in children-workers & suicidal is common
Mechanism	CNS : depression ↓ Na-K ATPase -- Peripheral : vasodilatation →false sensation of heat as HRC ↓ & Metabolism : ↓ NAD/NADH → hypoglycemia-fatty liver-metabolic acidosis	CNS depressant more than Al – git irritation – metabolic acidosis is 6 times severer- ocular toxicity (↓cytochrome oxidase in optic nerve → ischemia & anaerobic metabolism)	Ingestion-inhalation –skin -target organs are lungs-CNS so cause aspiration pneumonia and CNS| depression but indirect due to hypoxia	1- high affinity to hemoglobin →↓ association &dissociation 2- bind to myoglobin →myocardal depression & cytochrome oxidase 3- brain lipid perioxidation → irreversible neuronal dysfunct	Block cytochrome oxidase lead to cellular asphyxia (histotoxic anoxia)- no cyanosis (red) – O2 in arterial = O2 in venous Local corrosive effect	Anticholine esterase lead to increase in acetylcholine level activate muscurinic and nicotinic
C/P	*1- stage of excitation* : o.o5-o.15 % serum level : inhibition of centers which control judgement – euphoria *2- stage of incoordination :* 0.15-0.3% motor incoordinat (drunken gait- tremors of hands- slurred speech- ↓skills) Hiccough- diplopia-vomiting- flushed skin *3- stage of seizures-coma :* >o.5% seizures-shock- alcoholic smell – McEwen mpupil – coma RC depression	*1- visual* : optic nerve atrophy & irreversible blindness *2- metabolic acidosis* : tachypnea – air hungar-life threting hyperkalemia *3- GIt* : cramps –dehydration *4- CNS* : disorientation stupor –coma-convulsions – encephalopathy *5- respiratory depression* follows acidotic breathing *6- shock* depression of VMC – vomiting	*1- chemical pneumonia* : cough –dyspnea-tachypnea- cyanosis-edema – hemoptysis –shock *2- CN*S : dizziness – hyporefelxia-convulsions *3- GIT* : local irritation *4- erythema*- dermatitis – ocular irritation –arrythemia	*1- 20% COHb* :CNS : headache-CVS :dyspnea *2- 30%* : CNS : throbbing headache- CVS : dyspnea- tachapenea –GIT : N-V *3- 40%* : the above + Muscles incorodination (Pt fail to escape) *4- 50%* : flaring of symptoms : headache –sver drowsiness – arrhythmia-ischemia – pulmonary edema – syncope *5- 60%* : convulsions –coma death – blister formation	*CNS* : confusion –convulsions –coma with Cs : corneal glistening –charceterstic smeel –clenched jaw – cherry red color – cyanide cry *CVS* : hypotension – bradycardia *GIT* : if ingested : pain –N-V	*1- muscurinic activation :* bradycardia – bronchospasm – pinpoint pupil –SLUD syndrome *2- Nicotinic* : dfatigue- twitches –fasciculations – tremors –then paralysis in reapirtory muscules *3- central action* : irritation then depression in resp center
Cause of death	Central asphyxia	Central asphyxia		Resp & circulatory failure	Respiratory failure	1- central asphyxia & peripheral (spasm – paralysis) bronchospasm 2- dignosed from CP & decreased choline sterase level in blood
investigation	1- rapid : finger to nose – straight line- 2- chemical : breath analyzer (colorimetric test) – urine –blood – ketoacidosis -	1-serum methanol level 2- fudus examination & visual evoked potential	Chest X-ray & CBC	1- detect COHb level in blood by spectroscopic exam- gas chromatography 2- detect effect of ↑CO&↓O2 on tissues (usual)	1- cyanide blood level 2- blood PH	
D/D	Atropine toxicity					1- prophylactic 2- antidotes are : atropine sulfate 1-2mgiv /10 min till chest is clear –correction of brady & Oximes : PAM 1gmin saline IV infusion in1st 24-48 hrs 3- decontamination of skin 4- lavage by NaHco3
TREATMENT	1- lavage by NaHco3 2- No charcoal 3- forced alkaline dieresis by NaHco3 – hemodialysis 4- Anti : vit B6 5- Symptomatic : NaaHco3 IV for acidosis – 10-50 % dextrose solution IV for hypoglycemia – warm patient for hypothermia – fluid	1- lavage by NaHco3 2- No charcoal 3- forced alkaline dieresis by NaHco3 – hemodialysis 4- Antidote s: methanol -4MP ;both inhibit alcohol dehydrogenase –folinic acid : convert formic into co2-h2o 5-the symptomatic as alcohol	1- emesis is contraindicated 2- lavage is indicated if large amounts or contain toxic additives 3- decontamination of clothes –skin-eye withcopios tepid water or saline 4-symptomatic : antipyretics-antibiotics if infection occur bronchodilators atropine – c	1- bed rest & warmth ↓ O2 demand 2- ABCs 3- Oxygenation : fresh air if COHb < 15% & 100% O2 if COHb >15% & hyperbaric O2 if COHb ≥ 40 % 4- symptomatic : prednisolone 1mg /kg IV /4hr + mannitol 20% 1mg/kg IV for 20 min for cerebral edema & Bood	1- physiological antidotes : nitrate thiosulphate therapy – hydroxycobalamine vit B12 a- kelocyanar (dicobalt EDTA) – DMAP) 2- loacal ant i: charcoal- H2O2 – NA thiosulphate (oxidation) – repeat physiological antidotes after 1-2days	
OTHERS	Absorp “: major from intestin – minor from stomach/// Distri : all tissues pass BBB-placent /// Metabolism : 90-98 % in liver to acetyldehyde by dehydrogenase then to acetic acid then in krebs to Co2-Ho2 /// Exce: 2-10% unchanged in urine-breath-sweat-tearaa –bile-gastric	Absorption : gut-cutenous-ihhalation - //distribution : to optic nerve as well- it is cumulative //// metabolism : 90% in liver to formaldehyde then to formic acid which by folate is coverted to co2-H2o /// Excertion : mainly live r others as kidney –lun g		Complications : 1- pulmonary edema –pneumonia 2- parkinsonism –encephalopathy 3- rhabdomyolysis 4- alteration in liver enzymes 5 – ECG changes and renal failure		Complications : 1- organophosphorus intermediate syndrome after 1day – paralysis of muscles – postsynaptic neuromuscular dysfunction 2- delayed peripheral neuropathy : 1-5weeks – parathesia –cramps-toe drop-distal degeneration

Medical toxicology 1

	Salycilates	Paracetamol	Barbiturates	Benzodiazepines	TCA	Lithium
sources uses	Aspirin –cold preparations - topical as methyl salycilate- salcyslic acid Analgesic –antipyretic	One of coal tar derivative APAP - Analgesic antipyretic only	Pyrimidin deravatives Sedatives – hypnotics – anticonvulsant-anaesthetic	Anxiolytics –hypnotics	Imipramine – amitriptyline – desipramine – maprotiline – amoxapine –fluoxetine – sertaline -//depression –panic	Acute mania- depression – bipolar disorders
condition	Accidental in children as it cause hyperpyrexia in toxicity in elderly & suicidal in young	Accidental most common	Suicidal common – homi to facilitate repa	Accidental mainly	Accidental-suicidal	Accidental
Mechanism	Antiinflamatory –analgesic- antipyretic through inhibition of prostaglandins synthesis	Inhibiton on synthesis of central prostaglandins // in toxic dose produce toxic metabolite cause centilobular necrosis	Bind to GABA receptors increase inhibitory synaptic transmission	Bz receptors in alpha subunit of GABA receptors lead to its stimulation and increased inhibition	Neurotransmitter reuptake inhibition & recptor blockade cholinergic –alpha-histaminic – myocardial membrane depressant effect (quinidine)	Compete for NA-K-Mg –Ca& inhibit release of dopamine – norepinephrine
C/P	ASHGARTEN 2-allergy ;: rash-asthma – angionertic edema 3- salycilism : tinnitus-vetigo-deafness 4- hematology : bleeding due to prothrombin –platelets 5- - GIT irritation : erosion – ulceration –burning pain 6- Acid bas eimbalance : respiratory alkalosis followedby metabolic acidosis 7-renal : tubular necrosis- decreased perfusion 8-temp : hyperthermia 9- electrolyte imbalance 10-nervous : ccentral stimulati	1- **phase 1 :** 1 day ;git symptoms N-V-drowsiness 2- phase 2 : 2 days : apparent recovery pain tender – altered blood liver enzymes 3- phase 3 : fulminant liver failure(jaundice –coagulation defect –encephalopathy) in 3days 4- phase 4: 1 week : prognosis recovery in 3-6 months or death in sever cases	1- CNS : comawith cyanosis – ski bullae – muscle flaccidty – shock deep / hypothermia resp failure – confusion 2- CVS : shock 3- RESP : resp depression – pneumonia-non cardiogenic pulmonary edema 4- renal : renal failure 5- GIT : ↓ bowel sounds 6- Skin : blisters in hands-foot	1- CNS depression –coma 2- cardio collapse –resp depression – hypothermia	1- CNS : coma –delirium-seizures-myoclonus -ataxia – nystagmus 2- CVS : arrhythmia (sinus tachy-conduction delay-ventricular arrhythmia) – intial hypertension then hypotension 3- Anticholinergic effect : dry skin- dilated pupil -↓ bowel sounds -↓urine flow – hyperthermia	1- CNS : depression then coma 2- GIT : N-V-C-D 3- Renal : tubular atrophy 4- CVS: collapse 5- Endocrine : hypothyroidism – myxedema coma – osteoporosis
Cause of death	Central asphyxia- arrhythmia – renal failure –hemorrhage	Liver failure	Central asphyxia –collapse//// –pneumonia –renal failure	Central asphyxia		
investigation	2-blood salicylate level- coagulation profile- Xray stomach	Serum level	Serum concenteation sby gas chromatography – immunoassay		Plasma drug level	Blood lithium level – thyroid function tests
TREATMENT	1- MDAC –whole bowel irrigation 2- forced alkaline dieresis 3-symptomatic : IV NaHco3- Ivfluids- demulcent- diazepam – vit K –cold foment – glucose IV	1-MDAC – liversupport (dextrose-sorbitol) 2- specific : NAC : provide protective levels of glutathione –as early es posiple – oral – 140mg/kg	1-lavage by cuffed endotracheal tube up to 12 hrs 2- MDAC – forced alkaline dieresis	Flumazenil is specific antidote 3mg IV in isolate BZ over doose and in minutes	MDAC (enterohepatic circulation) – enhanced elimination is largrely ineffective --- ttt conduction disturbance (NaHco3- lidocaine) – diazepam –aiv fluids & vasoprssors that poses alpha activity –cold foment	1-Activated charcoal doesnot work 2 –hemodialysis is very effective 3 – Diuresis worsen intoxication - 4- hydration therapy with normal saline should be initiated 5- Antidote : sodium poly stern sulfonate SPS) cation exchange resin release na In exchange for LI

Medical toxicology 2

	Amphetamine	Phenothiazines	Ca Antagonist	Beta blockers	Theophylline	Antihistamines
sources uses	Short term ttt of obesity – narcolepsy – hyperkinesias in children		Angina-coronary spam – hypertension – migraine – arrhythmia	Angina-coronary spam – hypertension – migraine – arrhythmia- glaucoma	Bronchospasm –congestive HF –neonatal apnea as orrlly and SR preparations	Used for allergy related itching – cold preparations – motion sickness –sleep aid
condition	Accidental addict or medical oral or IV		Accidental-intential	Accidental medical ly	Accidentally In medical use	
Mechanism	Sympathomimetic –strong CNS stimulant (↑release - ↓uptake of catecholeamine)	1- receptor blockade : anti cholinergic-antiserotonin-antihistamine-antidopamine – antialpha1 2- Quinidine like action	Coronary and peripheral VD- reduced cardiac contractility – slowing of conduction – depress SA node	Beta adrenergic blockade → depresse myocardial contractility and conduction and if lipid soluble causes seizures-coma	Adenosine receptor antagonist - ↓ phosphodiesterase - ↑intracellular CAMP – release catecholeamines – stimulate beta receptors	H1 blocker – anticholinergic receptors except non sedating as astemazole &azatadine- stimulate or depress CNS - DIphenhydramine has membrane depressant and local anaesthestic
C/P	***Stage 1*** : restlessness-insomnia –irritability ***2- stage 2*** : hyperactivity – confusion –HTN-Tachy ***3- stage 3*** : delirium –mania-self injury – hyperpyrexia (amphetamine induced psychosis) ***4- stage 4*** : convulsions – coma collapse	1-***CNS*** depression of CTZ & RC & HRC & dopamine blockade → dystonic reaction & Akathesia & Parkinsinism & tardive dyskinsia & neuroleptic malignant syndrome) 2-***CVS*** : hypotension – arrhthymia –conduction abnormalities 3- ***Anticholinergic :*** dry-blind-hot-red-bladder	1- hypotension due to all the previous 2-Bradycaardia : 3- QRS duration is usually not affected due to noaffection of intraventricular conduction except verapamil prolong QT 4- NON cardiac : metabolic acidosis – hyperglycemia abnormal mental status –-N-V	***A- Cardiac*** : hypotension – bradycardia –AV block – shock-asystole ***2-CNS*** : convulsion –coma-repiratory arrest with propranolol and other lipid soluble drugs ***3- Bronchospasm*** ***4- hypoglycemia-***hperkalemia	***A) acute toxicity*** : vomiting –tremors anxiety seizures – tachycardia hypotension ventricular arrhythmia – hypokalemia hyperglycemia metabolic acidosis . ***B) chronic*** : tachycardia is common –seizuers may occur but others are rare	Similar to anticholinergic poisoning If diphenhydramine : QRS widening –myocardial depression
Cause of death	Hyperthermia – centralasphyxia –circulatory collapse		Cardiac arrhythmia and circulatory collapse			
investigation			1- serum drug level and in urine 2- glucose-oximetry	Level in blood and urine	Acute oral overdose obtain reapted levels every 2-4 hrs due to SR preparations more over in chronic the symptoms more important than conc	Detected in blood (not commonly available) and in the urine
D/D						
treatment	GIT decontamination only in the absence of seizures – forced acid diuressis but not done - Cool quite environment - to minimize stimuli-phenothiazines(direct antagonist for amphetamine) for psychosis –nitorprusside for HTN – diazepam for convulsions – salicylate & chloropromazine for hyperthermia	1-MDAC –emsis is contraindicated – hemodilysis is not recommended 2- symptomatic : dystonia (benzotropine)- TD (shift other neuroleptic) – NMS (rapid cooling –Bromcriptine (antidotefor dopamine)- benzodiazepine) – arrhythmia (NaHco3-lidocaine MgSO4)- hypotension (dopamine – alpha agonist)	1- specific antidotes : Ca cl 10%10ml IV or Ca gluconate revers depression of cardiac contracitility ?? glucagon – epinephrine –amrinone increase HR & BP // aminopyridine 2- whole bowel irrigation & MDAC 3- enhanced elimination is not effective	1- specific anti : glucagon – epinephrine for bradycardia and hypotension /// NAHCo3 for wide conduction defect //// isoproterenol infusion and Mg for ventricular tachycardia 2- enhanced elimination and MDAC both can work here	1- specific : propranolol 0.01-0.03 mg/kg IV or esmolol 25-50µg/kg/min 2 – whole bowel irrigation 3- enhanced elimination is so effective as it has small volume of distribution and better than MDAC .	1- Specific antidote : phystigmine as anticholinerginc poisoning – NaHCO3 for myocardial depression 2- enhanced elimination and MDAC are both not effective

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